

James Blake *et al.*
Appl. No. 09/733,239
Amdt. dated December 15, 2004
Reply to Office Action of June 15, 2004

PATENT

REMARKS/ARGUMENTS

Claims 1-28 are currently pending in the above-identified application. Claims 14-28 have been withdrawn by the Examiner as being drawn to a nonelected invention. With this amendment, claims 1-13 are amended. Support for these amendments is identified in the following remarks. No new matter is added by these amendments. Examination and reconsideration of the pending claims is respectfully requested.

Priority

The Examiner, alleging that copendency between the instant application and one of the prior applications is absent, states that the priority date of the instant application is December 8, 2004.

Attached hereto is a copy of the return postcard showing that a Notice of Appeal was filed in the previous case (USSN 08/462,749) on May 4, 2000, with an extension of time. The PTO-stamped copy of the postcard shows that the Notice of Appeal was received on May 8, 2000. The period for filing an appeal brief, request for continued examination, or continuation application is the date of receipt of the Notice of Appeal (postcard date) (*see, e.g.*, MPEP § 1206, stating that "the Office date of receipt of the notice of appeal (and not the date indicated on any Certificate of Mailing under 37 CFR 1.8) is the date from which [the] two month time period is measured"). Further, Applicants note that the instant application was filed with an extension of time (five months from July 8, 2000 to December 8, 2000) for filing an appeal brief for the prior case. Accordingly, the instant application was filed during the copendency of the prior application and is entitled to the claimed priority as set forth in the preliminary amendment filed July 13, 2001.

Specification

The Examiner has objected to the specification as allegedly lacking specific sequence identification numbers (SEQ ID NOs) for the disclosed sequences. Applicants note that a substitute specification, designating SEQ ID NOs for all disclosed sequences in both the specification and the claims, was filed with the Office on 21 April 2004. Withdrawal of the objection is respectfully requested.

Rejections under 35 U.S.C. § 101

Claims 1-14 stand rejected under 35 U.S.C. § 101 as allegedly directed to non-statutory subject matter, the Examiner stating that the claims do not require the claimed peptide be "isolated peptide." Independent claim 1 has been amended to recite a "composition comprising an isolated peptide" In view of this amendment, the present rejection is obviated.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-14 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Each of these rejections is addressed below.

"Immunoreactive"

The Examiner contends that it is unclear what is intended by the term "immunoreactive" in claims 1 and 8. Applicants respectfully traverse.

A claim is definite if one of ordinary skill in the art would understand the scope of the claim when read in light of the specification. *See North Am. Vaccine, Inc. v. American Cyanamid Co.*, 28 USPQ2d 1333, 1339 (Fed. Cir. 1993). In the present case, the application is directed, *inter alia*, to immunoassay methods using peptides that mimic epitopic regions of a

protein and are thus capable of binding antibodies to the protein. (*See, e.g.*, specification at page 8, lines 4-7, 14-16.) Therefore, the skilled artisan reading the specification would understand the term "immunoreactive" in claims 1 and 8 to refer to a peptide capable of binding antibodies to a protein. Accordingly, claims 1 and 8 are definite under 35 U.S.C. § 112, second paragraph.

While claims 1 and 8 are believed to be definite for the reasons set forth above, but solely in order to expedite prosecution of the instant application, claims 1 and 8 are amended as follows. Claim 1 is amended to recite "...said peptide immunoreactive having at least one epitope capable of binding antibodies to a protein comprising the epitope(s)" Claim 8 is amended to recite the "peptide of claim 1 which is ~~immunoreactive with~~ capable of binding antibodies to a retroviral transmembrane protein." Support for these amendments are found in the specification at, *e.g.*, page 8, lines 11-18. For the reasons set forth above, the skilled artisan reading claims 1 and 8 in light of the specification would understand the term immunoreactive to mean peptides capable of binding antibodies to a protein having one or more epitopes corresponding to the peptide. Accordingly, the present amendment does not change or narrow the scope of claims 1 and 8.

"Native protein"

The Examiner believes that it is unclear what is intended by the term "native protein" in claim 1. Applicants respectfully traverse.

As indicated above, the present application is directed, *inter alia*, to immunoassays for the detection of antibodies to one or more proteins in a biological sample. It is well-understood that the detection of such antibodies in a sample is indicative of the presence, in a subject from which the sample originated, of proteins having one or more epitopes that elicited the antibodies. Therefore, the skilled artisan reading the claims in light of the specification would understand the term "native" in claim 1 to refer to a protein having one or more epitopes capable of eliciting an antibody response against the protein.

While Applicants believe the term "native" to be clear, but in order to expedite prosecution of the instant application, Applicants have amended claim 1 to delete the term "native." Applicants further note that, in view of the amendment set forth above, claim 1 now recites "... antibodies to a protein comprising the epitope(s) [capable of binding the antibodies]" For the reasons set forth above, this amendment is commensurate with the understanding of the skilled artisan reading claim 1, as originally presented, in light of the specification. Accordingly, the present amendment does not narrow the scope of claim 1.

"Reversibly protected by chemically reversible means"

The Examiner believes that it is unclear what is meant by the term "reversibly protected by chemically reversible means." The Examiner states that from this recitation, it is unclear what the thiol groups "are being protected from." Applicants respectfully traverse.

As set forth above, a claim is definite where one of ordinary skill in the art would understand the scope of the claim when read in light of the specification. *See North Am. Vaccine*, 28 USPQ2d at 1339. Here, the present application is directed to, *inter alia*, peptide compositions with improved immunological reactivity by controlling the oxidative form of the peptide. (*See, e.g.*, specification at page 4, lines 15-22.) It is well-known that controlling the oxidative form of a peptide controls the formation of disulfide bonds between cysteine residues. Further, in accordance with the present invention as described in the specification, chemical protection of the cysteine thiols is utilized to, *inter alia*, prevent disulfide bond formation. (*See, e.g.*, specification at page 10, lines 19-22.) Thus, it would be clear to the skilled artisan that the thiol groups are protected from oxidative conditions that would induce formation of disulfide bonds. For these reasons, Applicants believe the phrase "reversibly protected by chemically reversible means" in claim 1 to be definite.

While claim 1 is definite for the reasons set forth above, Applicants have amended claim 1 to further expedite prosecution of the instant application. Claim 1 is amended to recite "... reversibly protected from oxidation" Support for this amendment is found in the specification at, *e.g.*, page 8, lines 24-27. For the reasons set forth above, this amendment is commensurate with the understanding of the skilled artisan reading claim 1, as originally presented, in light the specification. Therefore, the present amendment does not change or narrow the scope of claim 1.

"At least about"

The Examiner believes that it is unclear what is meant by the term "at least about." Claims 1 and 7 have been amended to delete the term "about."

"Further comprising a Cys residue"

The Examiner contends that the phrase "further comprising a Cys residue" in claim 4 is indefinite because "it is unclear from the claim if Applicant is intended to include a third cysteine into the sequence or not, because claim 1, which claim 4 depends on, [already recites] cysteine residues." Applicants respectfully traverse.

Claim 4 recites, in pertinent part, "... further comprising a Cys residue at the N terminus which is not protected from oxidation" (emphasis added). For reasons set forth below in response to the Examiner's remarks regarding the term "N-terminus," it would be clear to the skilled artisan that the phrase "which is not protected from oxidation" modifies the Cys residue recited in claim 4. Claim 1 recites two Cys residues that are "protected by chemically reversible means." Further, for the reasons set forth above in response to the Examiner's remarks regarding the phrase "reversibly protected by chemically reversible means," it would clear to the skilled artisan that the two Cys residues recited in claim 1 are protected from oxidation. Accordingly, it

would be clear to the artisan reading the claims that the Cys residue in claim 4 is a third Cys residue, *i.e.*, a Cys residue in addition to those already recited in claim 1. Therefore, Applicants believe claim 4 to be definite under 35 U.S.C. § 112, second paragraph.

While claim 4 is definite for the reasons set forth above, but in order to expedite prosecution of the instant application, claim 4 has been amended to recite "further comprising a third Cys residue" For the reasons set forth above, this amendment is commensurate with the understanding of the skilled artisan reading claim 4, as originally presented, in light of claim 1 and the specification. Therefore, the present amendment does not change or narrow the scope of claim 4.

"N-terminus"

The Examiner believe that it is unclear in claims 4 and 10 to "which N-terminus" the Cys residue is attached. Applicants respectfully traverse.

The term "N-terminus" is well-understood in the art to refer to the amino (-NH₂) group, or the amino acid residue containing it, at one end of a polymer of amino acids. The term is not used, as the Examiner seems to suggest, to refer to individual amino acids within a peptide, unless the term is used in the context of a particular region or fragment within the peptide. Further, the specification describes embodiments of the invention in which "amino acid arms" are provided "at the C- and/or N-terminus of the peptide" (Specification at page 13, lines 22 and 23.) The specification additionally describes an embodiment in which a Cys residue is the "N-terminal residue of the arm" (and thus the N-terminal residue of the peptide). (*See* specification at page 14, lines 2-6.) Accordingly, Applicants believe the meaning of the term "N-terminus" in claims 4 and 10 to be definite under 35 U.S.C. § 112, second paragraph.

While the term "N-terminus" in claims 4 and 10 is definite for the reasons set forth above, Applicants have amended claims 4 and 10 to further expedite prosecution of the instant application. Claims 4 and 10 have been amended to recite "... N-terminus of the peptide" Support for this amendment is found in the specification at, *e.g.*, page 13, lines 22-24. For the reasons set forth above, this amendment is commensurate with the understanding of the skilled artisan reading claims 4 and 10, as originally presented, in light of the specification. Therefore, these amendments do not change or narrow the scope of claims 4 and 10.

"Cys-Gly-Gly"

The Examiner believes that the phrase "wherein the N-terminal amino acids comprise Cys-Gly-Gly" in claim 5 is not clear. The Examiner states it is not clear which N-terminal is meant by the claim. The Examiner further contends that it is unclear if the Cys recited in the fragment "Cys-Gly-Gly" is directed at the first, second, or third Cys residue, or another Cys residue. Applicants respectfully traverse.

First, for the reasons set forth above with respect to the meaning of "N-terminus," and in further view of the specification, the skilled artisan would understand the phrase "wherein the N-terminal amino acids comprise Cys-Gly-Gly" to mean that a "Cys-Gly-Gly" arm at the N-terminus of the peptide. Again, the specification describes embodiments of the invention in which "amino acid arms" are provided "at the C- and/or N-terminus of the peptide" (Specification at page 13, lines 22 and 23.) The specification additionally describes an embodiment in which a Cys residue is the "N-terminal residue of the arm" (and thus the N-terminal residue of the peptide). (*See* specification at page 14, lines 2-6.)

Further, it is a well-known in the art that polymers of amino acids are always written with the N-terminal amino acid toward the left. Here, the Cys residue is at the leftmost amino acid residue of as recited in "Cys-Gly-Gly." Accordingly, this Cys residue is the N-

terminal amino acid of the Cys-Gly-Gly arm. Also, because the Cys-Gly-Gly arm is at the N-terminus of the peptide, the skilled artisan would understand that this Cys residue is at the N-terminus of the peptide itself. Therefore, because claim 4, from which claim 5 depends, recites a Cys residue at the N-terminus, the skilled artisan would also understand the Cys residue of claim 5 to correspond to the Cys residue recited in claim 4.

For the reasons stated above, Applicants believe the meaning of claim 5 to be definite under 35 U.S.C. § 112, second paragraph.

While Applicants believe claim 5 to be definite, but in order to further expedite prosecution of the instant application, claim 5 has been amended to recite "~~wherein the N-terminal amino acids~~ N-terminus sequence of the peptide is comprise Cys-Gly-Gly." For the reasons set forth above, this amendment is commensurate with the understanding of the skilled artisan reading claim 5, as originally presented, in light of the specification. Therefore, this amendment does not change or narrow the scope of claim 5.

"C-terminus"

The Examiner contends that the term "C-terminus" in claim 6 lacks clarity. Applicants respectfully traverse.

The term "C-terminus" is well-understood in the art to refer to the carboxyl (-COOH) group, or the amino acid residue containing it, at one end of a polymer of amino acids. The term is not used, as the Examiner seems to suggest, to individual amino acids within a peptide. Accordingly, Applicants believe the meaning of the term "C-terminus" in claim 6 to be definite under 35 U.S.C. § 112, second paragraph.

While the term "C-terminus" in claim 6 is definite for the reasons set forth above, Applicants have amended claim 6 to expedite prosecution of the instant application. Claim 6 has been amended to recite "... amino acid at the C-terminus of the peptide" For the reasons set forth above, this amendment is commensurate with the understanding of the skilled artisan reading claim 6, as originally presented, in light of the specification. Therefore, this amendment does not change or narrow the scope of claim 6.

Location of added Cys in claim 11

The Examiner believes that it is unclear if the newly added Cys, which is not protected from oxidation, "is at the N-terminus of the peptide prior to the addition of other amino acids, including the instant cys; or after the addition of other amino acids" Applicants respectfully traverse.

Claim 11 recites a peptide that includes amino acids added to enhance immunospecific reactivity of the peptide. One of the added amino acids is a Cys residue not protected from oxidation. Claim 11 further recites that the Cys residue not protected from oxidation is the N-terminal residue.

First, because the recited Cys residue is one of the amino acids added to enhance immunospecific reactivity, it is unclear to Applicants how the skilled artisan would possibly interpret the claim to mean that the added Cys residue is at the N-terminus of the peptide before the addition of the Cys residue.

Further, as set forth above, the term "N-terminus" is well-understood in the art to refer to the -NH₂ group, or the amino acid residue containing it, at one end of a polymer of amino acids. Accordingly, because claim 11 recites a peptide, the skilled artisan reading the claim would understand the phrase "wherein the Cys not protected from oxidation is the N-

terminal residue," as recited in the claim, to mean that the Cys residue, not protected from oxidation, is located at the N-terminus of the recited peptide itself.

While Applicants believe claim 11 to be definite for the reasons above, but in order to expedite prosecution of the instant application, claim 11 has been amended to recite "wherein the third Cys not protected from oxidation" Claim 11 is also amended to recite "... N-terminal residue of the peptide." Support for this amendment is found in the specification at, *e.g.*, page 13, lines 22-24. For the reasons set forth above, these amendments are commensurate with the understanding of the skilled artisan reading claim 11, as originally presented, in light of the specification. Therefore, these amendments do not change or narrow the scope of claim 11.

Cys-Gly-Gly residue in claim 12

The Examiner contends that it is unclear if "Cys-Gly-Gly," as recited in claim 12, includes the Cys residue that is newly added and not protected from oxidation. Applicants respectfully traverse.

As set forth above, the skilled artisan would know that the Cys residue as recited in claim 11, upon which claim 12 depends, is the N-terminal residue of the peptide. Further, because it is a well-established convention in the art that polymers of amino acids are written with the N-terminal amino acid at the left, the skilled artisan would understand that the Cys residue of "Cys-Gly-Gly" is at the N-terminal end of recited fragment. Accordingly, since claim 12 recites that "Cys-Gly-Gly" is the N-terminus sequence, the skilled artisan would understand the Cys residue of "Cys-Gly-Gly" is the N-terminal amino acid of the peptide and, therefore, the same Cys residue as recited in claim 11.

While Applicants believe claim 12 to be definite for the reasons above, Applicants have amended claim 12 to expedite prosecution of the instant application. Claim 12 has been amended to recite "wherein the N-terminus sequence of the peptide is Cys-Gly-Gly," thereby further clarifying that "Cys-Gly-Gly" is the N-terminal sequence of the peptide itself (and, therefore, by virtue of the convention of writing peptides with the N-terminus toward the left, that the recited Cys of the "Cys-Gly-Gly" arm is the N-terminal amino acid of the peptide). For the reasons set forth above, this amendment is commensurate with the understanding of the skilled artisan reading claim 12, as originally presented, in light of the specification. Therefore, this amendment does not change or narrow the scope of claim 12.

Lack of antecedent basis rejections

The Examiner has set forth numerous "antecedent basis rejections" for recitation of the limitation "N-terminus," "N-terminal," or "C-terminus" in claims 4-6, 10, 11, and 13. Applicants respectfully traverse.

The lack of explicit antecedent basis for terms does not, by itself, render a claim indefinite. MPEP § 2173.05(e). As noted above, a claim is definite if the scope of the claim would be reasonably ascertainable by those skilled in the art. *See id.*, citing *Ex parte Porter*, 25 USPQ2d 1144, 1145 (Bd. Pat. App. & Inter. 1992). Further, "[i]nherent components of elements recited have antecedent basis in the recitation of the components themselves." MPEP § 2173.05(e) (stating that the limitation "the outer surface of said sphere" would not require an antecedent recitation that the sphere has an outer surface). *See also Bose Corp. v. JBL, Inc.*, 61 USPQ2d 1216, 1218-19 (Fed. Cir. 2001) (holding that recitation of "an ellipse" provided antecedent basis for an "ellipse having a major diameter" because "[t]here can be no dispute that mathematically an inherent characteristic of an ellipse is a major diameter").

In view of the above, the terms N-terminus and C-terminus in claims 4-6, 10, 11, and 13 are definite under 35 U.S.C. § 112, second paragraph. Each of the claims at issue are directed to a composition comprising peptides. It is well-understood in the art that a peptide has an N-terminus and a C-terminus. "N-terminus" and "C-terminus" are, therefore, inherent components of the peptides recited in the claims. Accordingly, these terms have antecedent basis in the recitation of the terms themselves.

Applicants also note that the claims have been amended, as set forth above, to recite N-terminus/N-terminal residue/C-terminus "of the peptide." These amendments further clarify that which would be understood by the skilled artisan reading the claims, *i.e.*, that the terms N-terminus or C-terminus refer to the previously recited peptide.

In view of the above, claims 1-14 are definite. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejections of claim 1-14 under 35 U.S.C. § 112, second paragraph.

Rejections under 35 U.S.C. § 102

Claims 1-13 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Blake *et al.* (WO 90/15071), published December 13, 1990.

Applicants note that, for the reasons previously set forth, the instant application is entitled to the claimed priority, which includes, *inter alia*, USSN 07/532,429, filed June 4, 1990. Therefore, Blake *et al.*, published December 13, 1990, is not prior art to the instant application. Withdrawal of the instant rejection is respectfully requested.

Other Amendments

Claim 1 has been amended to claim certain aspects of the present invention with greater particularity. Claim 1 has been amended to recite that the isolated peptide of the composition is "immobilized on a solid phase." Support for this amendment is found in the specification at, *e.g.*, page 5, lines 4-6; and page 10, lines 24-26. Claim 1 has also been amended to recite "... wherein a substantial portion of the composition comprising the immobilized peptide comprises peptide having an intramolecular disulfide bond between the two Cys residues." Support for this amendment is found in the specification at, *e.g.*, page 10, lines 32-36.

For the sake of clarity, in view of the amendment to claim 1 to recite "a ~~peptide~~ composition comprising an isolated peptide ..., corresponding amendments have been made to dependent claims 2-13 to recite "[t]he ~~peptide~~ composition of claim [1]"

James Blake *et al.*
Appl. No. 09/733,239
Amdt. dated December 15, 2004
Reply to Office Action of June 15, 2004

PATENT

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.

Respectfully submitted,

Dated: 15 December 2004

By:

Brian W. Poor
Brian W. Poor
Reg. No. 32,928

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 206-467-9600
Fax: 415-576-0300
BWP:jms
60246393 v1